REMARKS

The present invention is directed to methods and compositions for the treatment of prostate cancer, which contain mycobacterial DNA or mycobacterial cell wall complex. Claims 32-65 are currently pending. Claims 32-56 have been amended to correct the numbering and Claims 57-65 have been cancelled.

Support for the amendments to the claims is found throughout the specification. No new matter has been added.

Claim Objections

The Examiner raised a formal objection to the numbering of the claims, stating that the pending claims were not numbered in accordance with 37 C.F.R. 1.126. The application consisted of Claims 1-25, but Applicants filed an amendment on March 20, 2002 numbering new Claims 32-65. To facilitate examination of this application, the Examiner renumbered Claims 32-65 as Claims 26-59. Applicants wish to confirm that renumbered Claims 26-59 are pending and have amended the claims to reflect the correct numbering.

Rejection of Claims 26-35, 38-47, 49-56, 58 and 59 under 35 U.S.C. § 102 (b)

The Examiner rejected Claims 26-35, 38-47, 49-56, 58 and 59 under 35 U.S.C. § 102 (b) as being anticipated by Morales et al., J. Urology, 153:1706-10 (1995). The Examiner asserts that Morales discloses every element of the claimed invention. To support these assertions, the Examiner relies on page 1706 and Figure 2 of Morales.

Applicants respectfully traverse the Examiner's rejection of Claims 26-35, 38-47 and 49-50.

Anticipation of a patent requires the presence in a single prior art reference of each and every element of the claimed invention, as arranged in the claims. *See Novo Nordisk v. Becton Dickinson & Co.*, 96 F.Supp.2d 309, 312 (S.D.N.Y. 2000)(citing *Lindeman Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452,

1458 (Fed. Cir. 1984)). It is incumbent on the Examiner to identify where every facet of the claimed invention is disclosed in the prior art reference. *See Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1462 (C.C.P.A. 1990).

Applicants respectfully assert that the Examiner has failed to identify where every facet of the claimed invention is disclosed in Morales. The Examiner states that the first column on page 1706 of Morales teaches a method of treating prostate cancer comprising administration of a composition comprising mycobacterial DNA (B-DNA) from *M. phlei* and a pharmaceutically acceptable carrier, such as oil microdroplets. Unlike the claimed invention, Morales does not teach the use of *M. phlei* DNA or the use of *M. phlei* DNA cell wall complex.

Applicants' review of Morales reveals that the reference actually describes the use of a fractionated and deproteinized emulsion of *M. phlei* cell walls. Pending claims 51-59 (previously numbered as Claims 57-65) are directed to a composition comprising mycobacterial cell walls and a pharmaceutically acceptable carrier; therefore, Applicants have cancelled Claims 51-59.

The Examiner further states that the first column on page 1706 of Morales teaches a method of treating prostate cancer comprising administration of a composition comprising mycobacterial DNA (B-DNA) and a pharmaceutically acceptable carrier, wherein the pharmaceutically acceptable carrier is *M. phlei* cell walls. However, Morales does not teach that *M. phlei* cell walls can be a pharmaceutically acceptable carrier for *M. phlei* DNA. Rather, Morales teaches that oil microdroplets may be a pharmaceutically acceptable carrier for *M. phlei* cell walls.

The Examiner also states that the first column on page 1706 of Morales teaches that *M. phlei* DNA is preserved and complexed to *M. phlei* cell walls. The Examiner relies on the doctrine of inherency to support this assertion, stating that the *M. phlei* cell wall would inherently have *M. phlei* DNA preserved and complexed to the cell wall unless the cell wall was specifically treated with nucleases to remove the DNA.

Morales discloses the use of a fractionated and deproteinized emulsion of *M. phlei* cell walls, but Morales does not comment on the presence or absence of DNA in this emulsion. It is possible that the *M. phlei* cell walls used in the Morales study contained DNA, but it is also possible that the cell walls were treated with nucleases. Inherency may not be established by probabilities or possibilities. *See In re Oelrich and Divigard*, 212 U.S.P.Q. 323 (C.C.P.A. 1981). The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *See id.* Therefore, Applicants respectfully assert that the Examiner's reliance on the doctrine of inherency is inappropriate in this case.

Further, Morales does not disclose the use of *M. phlei* DNA, and to conclude that the cell walls used by Morales contained DNA would be pure speculation. Anticipation cannot be predicated on mere conjecture as to the characteristics of a prior art product. *See W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983).

In view of the foregoing remarks and amendment, Applicants respectfully submit that Claims 26-35, 38-47, and 49-50 are novel in view of Morales and request that this rejection be withdrawn.

Rejection of Claims 26-59 under 35 U.S.C. § 103 (a)

The Examiner rejected Claims 26-59 under 35 U.S.C. § 103 (a) as being unpatentable over Morales in view of Filion et al., Blood, 90(10), Suppl. 1:p.58B (1997). The Examiner states that Filion teaches that *M. phlei* cell wall complex is an antitumoral agent that induces IL-12 and that it would have been obvious to one of skill in the art to use the method of Morales to induce IL-12 production to treat prostate cancer. The Examiner further states that one of ordinary skill in the art would have been motivated to combine the cited references since Filion states "IL-12 synthesized in response to this DNA [*M. phlei* DNA] may be in part responsible for the antitumor activity of *M. phlei* MCC."

Applicants respectfully traverse this rejection.

Applicants respectfully submit that the claimed invention would not have been obvious to one of skill in the art for the following reasons. First, the Examiner states that it would have been obvious to combine Morales and Filion to treat prostate cancer. Morales discusses the use of mycobacterial cell walls to treat prostate cancer. The claimed invention does not recite the use of mycobacterial cell walls for treating any disease. Filion states that mycobacterial cell wall complex has antitumor activity, but Filion does not specify that mycobacterial cell wall complex can be used for tumors of the prostate. Filion discusses at length that mycobacterial cell wall complex induces IL-12 production in murine monocytes, murine macrophages, or human THP-1 monocytic cells. Therefore, Filion suggests the use of mycobacterial cell wall complex for treating leukemia, but does not suggest the use of mycobacterial cell wall complex for treating prostate cancer.

As is well known to those skilled in the art, the field of cancer treatment is not one that is composed of predictable or reliable treatments. Indeed it is not uncommon for a particular therapeutic regimen to be effective only for certain cancers, and many times for only certain patients. Many times, a treatment that may have been effective previously may cease to have any beneficial value when administered again. Those skilled in the art would agree that the teaching of a particular therapeutic composition for a particular cancer would not necessarily lead one to assume that the same composition would be effective for the treatment of another cancer. Accordingly, the teaching of cancer treatment compositions in Morales and Filion do not make the claimed invention obvious.

Second, the method taught by Morales does not disclose the use of DNA for treating prostate cancer. The claimed invention recites the use of mycobacterial DNA or the use of mycobacterial cell wall complex, which includes specific amounts of DNA (*See* Specification, p. 13, lines 5-11). Filion mentions that *M. phlei* DNA contributes significantly to the ability of mycobacterial cell wall complex to induce 1L-12 production. However, Filion does not specify amounts of mycobacterial DNA required for causing antineoplastic activity in prostate cancer.

Finally, neither Filion nor Morales teaches a composition that may be used to treat androgen-sensitive and androgen-insensitive prostate cancer cells. Morales states that mycobacterial cell walls were used on prostate cancer cells that were a mixed population of androgen-sensitive and androgen-insensitive cells. Morales, however, fails to determine if the androgen-sensitive and androgen-insensitive cells respond differently to treatment with mycobacterial cell walls. The claimed invention, on the other hand, treats both androgen-sensitive and androgen-insensitive prostate cancer cells. (*See* Specification, Examples 12-15).

In light of the foregoing remarks, Applicants respectfully submit that the claimed invention would not have been obvious in light of Morales and Filion and request that this rejection be withdrawn.

Version of Claim Amendments with Markings to Show Changes

[32] 26. (Amended) A method of treating prostate cancer comprising administration of a composition comprising mycobacterial DNA (B-DNA) and a pharmaceutically acceptable carrier to an animal or human having prostate cancer in an amount effective to have an antineoplastic effect on prostate cancer in the animal or human having the prostate cancer.

[33] 27. (Amended) The method of Claim [32] 26, wherein the mycobacterial DNA is obtained from *M. smegmatis, M. kansaii, M. fortuitum, M. tuberculosis, M. bovis, M. vaccae, M. avium* or *M. phlei.*

[34] 28. (Amended) The method of Claim [32] 26, wherein the mycobacterial DNA (B-DNA) is obtained from *M. phlei.*

[35] 29. (Amended) The method of Claim [32] 26, wherein the pharmaceutically acceptable carrier is mycobacterial cell wall (BCC).

[36] 30. (Amended) The method of Claim [35] 29, wherein the mycobacterial DNA (B-DNA) is preserved and complexed on the mycobacterial cell wall (BCC).

[37] 31. (Amended) The method of Claim [32] 26, wherein the pharmaceutically acceptable carrier is *M. phlei* cell wall (MCC).

[38] 32.(Amended) The method of Claim [37] 31, wherein *M. phlei* DNA is preserved and con

[39] 33.(Amended) The method of Claim [32] 26, wherein the prostate cancer is hormone-sens

[40] 34.(Amended) The method of Claim [39] 33, wherein the hormone is an androgen.

[41] 35. (Amended) The method of Claim [40] 34, wherein the androgen is testosterone.

[42] 36. (Amended) The method of Claim [32] 26, wherein the antineoplastic effect is inhibition of proliferation of cancer cells in the prostate, induction of apoptosis in the cancer cells in the prostate, induction of cytokine synthesis in the cancer cells in the prostate, or induction of cytokine synthesis by immune system cells in the prostate.

[43] 37.(Amended) The method of Claim [42] 36, wherein the cytokine is IL-12 or TNF-α

[44] 38. (Amended) The method of Claim [32] 26, wherein the pharmaceutically acceptable carrier is a solid carrier, a liquid carrier, or combination of a solid and liquid carrier.

[45] 39. (Amended) The method of Claim [32] 26, further comprising administration of anti-androgenic agents, chemotherapeutic agents, steroids, or immunological agents.

[46] 40.(Amended) A method of treating prostate cancer comprising administration of a comp effective to have an antineoplastic effect on prostate cancer in the animal or human having the prostate cancer.

[47] 41.(Amended) The method of Claim [46] 40, wherein the mycobacterial DNA is obtained

[48] 42.(Amended) The method of Claim [46] 40, wherein the mycobacterial DNA is obtained

[49] 43. (Amended) The method of Claim [46] 40, wherein the mycobacterial cell wall is *M. phlei* cell wall (MCC).

[50] 44. (Amended) The method of Claim [46] 40, wherein the prostate cancer is hormone-sensitive prostate cancer.

[51] 45. (Amended) The method of Claim [50] 44, wherein the hormone is an androgen.

[52] 46. (Amended) The method of Claim [51] 45, wherein the androgen is testosterone.

[53] 47. (Amended) The method of Claim [46] 40, wherein the antineoplastic effect is inhibition of proliferation of cancer cells in the prostate, induction of apoptosis in cancer cells in the prostate, induction of cytokine synthesis by cancer cells in the prostate, or induction of cytokine synthesis by immune system cells in the prostate.

[54] 48. (Amended) The method of Claim [53] 47, wherein the cytokine is IL-12 or TNF-α.

[55] 49. (Amended) The method of Claim [46] 40, wherein the pharmaceutically acceptable carrier is a solid carrier, a liquid carrier, or a combination of a solid and liquid carrier.

[56] 50. (Amended) The method of Claim [46] 40, further comprising administration of anti-androgenic agents, chemotherapeutic agents, steroids, or immunological agents.

Conclusion

In light of the amendments and the above remarks, Applicants are of the opinion that all 26-50 are now in condition for allowance. Applicants further submit that present claims are not anticipated over the art of record, and earnestly solicit an early and favorable notice of allowability.

Should the Examiner believe that anything further is necessary to place the application in better condition for allowance, the Examiner is respectfully requested to contact Applicants' representative at the telephone number listed below.

No additional fees are currently believed due; however, please charge any additional fees or credit any overpayment to Deposit Account No. 11-0855.

Respectfully submitted,

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